UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/639,690	08/16/00	BENSON	A 101997-5

021125
NUTTER MCCLENNEN & FISH LLP
ONE INTERNATIONAL PLACE
BOSTON MA 02110

HM12/0615

EXAMINER	
GANSHEROFF, I	
ART UNIT	**PAPER NUMBER**
1636	9

DATE MAILED: 06/15/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev.11/00)

1- File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/639,690	BENSON, ANDREW K.	
	Examiner	Art Unit	
	Lisa Gansheroff	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,14-21 and 23-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,14-21 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☒ Other: *detailed action* .

DETAILED ACTION

Pending claims: 1-9, 14-21, 23-25.

This action is in response to: Amendment filed 30 April 2001.

Drawings

The replacement set of formal drawings submitted with the Amendment are acceptable and have been stampled "Approved" by the Draftsman.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 14 and 17-19 stand rejected, and claims 20 and newly-submitted claims 23-25 are rejected under 35 U.S.C. 102(e) as being anticipated by Heynecker (U.S. Patent 6,057,100), for the reasons made of record in the Office Action of 20 Dec. 2000 and for the reasons presented below regarding claims 23-25. Claim 20 has been added to this rejection because Heynecker teaches pathogenic bacteria and viruses, which are inherently mammalian colonizing species.

In response to the rejection over Heyneker, Applicants arguments, as follow, have been fully considered but they are not persuasive (except with respect to the multiple probe

oligonucleotides for a single species) for the following reasons. Applicants argue that Heyneker's basic concept relates to single-oligonucleotide stripes being more efficiently treated with small quantities of available probe material and distinguishes his invention from prior art requiring use of short probe sequences, and so forth. These arguments do not address the teachings of Heyneker which anticipate the claimed invention. Applicant also argues that Heyneker does not appear to teach multiple probe oligonucleotides for a single species; those claims which have been amended to recite this limitation (claim 1 and dependent claims) have been withdrawn from this rejection, as evidenced above. Applicant also argues that Heyneker simply detects the presence or absence, but does not mention a distribution or employing databases or correlation techniques or data mining. In response, it is noted that Heyneker teaches determining the presence, absence, or relative amounts of the target sequence in a sample (column 8). Such information would form an output distribution which is not distinguished from the limitations of the instant claims. The database and data mining limitations are in claims that were addressed by the rejections under 35 USC 103(a). Applicant also argues that Heyneker does not suggest selecting a set of oligonucleotides and probes such that they will not have crossreactivities; in response, while this would be inherent in any working method employing multiple oligonucleotides, it is also a feature which is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant also argues that Heyneker assumes that samples will be treated as is known in the art; in response, Applicants also treat samples as known in the art: the instant claims do not suggest novel methods for culturing or DNA extraction or PCR. With respect to newly-added

claims 23-25, it is also noted that any method employing multiple sequences simultaneously used for hybridization would inherently need to be assessed for efficient probe hybridization and detection, and for sensitivity and cross reactivity; otherwise, the method would not work due to some sequences on the array not hybridizing or cross-reacting (presumably Applicant means with species for which the sequence is not an intended probe). Further, as Heyneker suggests basing washing the array under conditions depending on the length and composition of the oligonucleotides (column 9), Heyneker is clearly aware of the technical aspects of hybridization.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14-21 stand rejected, and newly-submitted claims 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heyneker et al. as applied to claims 14, 17-20, and 23-25 above, and further in view of Anderson, Bruckner-Lea et al., Bergeron et al., Nakayama et al., and Tauxe, for the for the reasons made of record in the Office Action of 20 Dec. 2000.

In response to the rejection of claims 14-21 under 35 USC 103(a), Applicant argues that the Bergeron patent teaches probe arrays that are specifically designed to test for multiple pathogens, but that it does not suggest the output of distributions, the building of various distribution databases and their use in identifying extrinsic conditions such as process or food history or other parameters. (While Applicants do not argue that the cited references do not teach multiple probe oligonucleotides for a single species, it is not clear whether Applicants observed some clear teaching of such in the cited references, or simply did not address this new limitation of claim 1. A new rejection under 35 USC 103(a) is presented below, nonetheless, with a clear teaching of this newly-added limitation.) These arguments have been fully considered but they are not persuasive because the other cited references teach the limitations not discussed by Bergeron, as noted in the previous Office Action. See, for example, the Anderson et al. and Tauxe references. It appears that Applicants are suggesting that they are the first to contemplate the use of databases for storing and gleaning information about infectious disease (such as foodborne pathogens); this is not so.

Claims 1-9 and 14-21 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heyneker et al., Anderson, Bruckner-Lea et al., Bergeron et al., Nakayama et

al., and Tauxe, as applied to claims 14-20 and 23-25 above, and further in view of Megerle (U.S. Patent 5,874,046).

Megerle teaches detection with an array of oligonucleotides of target microorganisms, and teaches that to offer independent confirmation of the detection of a target microorganism, a plurality of oligonucleotides may be synthesized that are complementary to different segments of the target microorganism's DNA (see column 9). Megerle also teaches output distributions that include the presence of an organism and its location; such distributions are linked to a network so that decisions could be made based on this information (see column 4).

At the time of the invention of the instant application, the ordinary artisan would have been motivated to combine the teachings of Megerle regarding the use of multiple probes to different segments of a microorganism's DNA with the teachings of the other cited references regarding detection of microorganisms with probe arrays because Megerle teaches that this offers confirmation of the detection of a target microorganism, and thus would improve the confidence level in the data obtained. Success would have been expected.

Claims 14, 17-20, and 23-25 are rejected under 35 U.S.C. 102(e) as being anticipated by Balch (U.S. Patent 6,083,763).

Balch teaches multiplexed molecular analysis of samples with probe arrays. Balch teaches preparation of an array of probes from a plurality of different species (see for example column 38, lines63-67), sample preparation including extracting target molecules from the sample (see for example column 10 lines 54-58), PCR amplification if necessary (see for

example column 35 lines 1-11), and hybridizing the DNA (after labeling) to the probe array. The samples for the method can be air, water, and food samples or patient samples for detection of multiple microorganisms and determination of a microbial spectrum of the amount and type of microorganisms, such as pathogenic microorganisms, present in the sample. See for example columns 33-37 and 38-39, Examples III and VII. The process can also be automated with fluidics (see column 5 , lines 51-67 to column 6, line43).

Claims 1-9, 14-21, and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balch, as applied to claims 14, 17-20, and 23-25 above, in view of Megerle (U.S. Patent 5,874,046), and further in view of Anderson, Bruckner-Lea et al. (1999), Bergeron et al., Nakayama et al., and Tauxe (1997) (of record).

As noted above, Megerle teaches detection with an array of oligonucleotides of target microorganisms, and teaches that to offer independent confirmation of the detection of a target microorganism, a plurality of oligonucleotides may be synthesized that are complementary to different segments of the target microorganism's DNA (see column 9). Megerle also teaches output distributions that include the presence of an organism and its location (see above.

The teachings of Anderson, Bergeron et al., Nakayama et al., and Tauxe are described in the previous Office Action. Briefly:

Anderson et al. teach oligonucleotide probe arrays and automated fluidics for hybridization methods of nucleic acid based diagnostic and other applications. Anderson et al. teach data gathering methods.

Bruckner-Lea et al. teach methods involving automated fluidics in sample preparation, nucleic acid purification from environmental and food processing samples.

Bergeron et al., like Balch, also teach methods of detection of simultaneously more than one bacterial species with oligonucleotide probes. That is, multiple species analysis has been proposed before by several inventors.

Nakayama et al. teach oligonucleotide primers complementary to sequences encoding genes related to pathogenicity and also teach culturing.

Tauxe review foodborne diseases, including information systems to detect when and where contamination occurs in the production process. Tauxe also reviews electronic surveillance strategies in which data is used to monitor outbreaks and trace trends in foodborne disease; that is, Tauxe teaches databasing information and mining databases.

At the time of the invention of the instant application, the ordinary artisan would have been motivated to detect a plurality of species in food products and in other samples, since many microorganisms can contaminate food (or other samples) and cause disease. One would have been motivated to use a probe array as taught by Balch to obtain an output distribution of the types and number of microorganisms present or any other data determinable by the multiplex methods of Balch, to use automated methods to save time and effort as taught by Balch and Anderson, to detect multiple sequences for each species as taught by Megerle to confirm detection data, to use genes involved in pathogenicity for probe detection as taught by Nakayama, and to store the information in a database (as opposed to throwing it away or writing it down laboriously with pencil and paper) for easy retrieval and referral later, and for comparing against other databased information for such purposes as identifying a point in food preparation

process at which contamination is occurring (as in the HACCP process reviewed by Tauxe) or for such purposes as contributing to and mining the information in electronic surveillance networks such as FoodNet (reviewed by Tauxe) to monitor outbreaks, infections, and other public health information. Success would have been expected.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites "a note indicating required action". It is not clear what is to be encompassed by the term "required action", and thus the metes and bounds of the claim are indefinite.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa J. Gansheroff whose telephone number is (703) 605-1203. The examiner can normally be reached 9 AM - 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached at (703) 308-0447. The fax phone number for the organization where this application or proceeding is

assigned is (703) 308-4242 for regular communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Dianiece Jacobs whose telephone number is (703) 305-3388 or to the receptionist whose telephone number is (703) 308-0196.

LG
June 6, 2001

JAMES KETTER
PRIMARY EXAMINER